105. (New) A humanized immunoglobulin according to any one of claims 102 through 104, wherein said humanized immunoglobulin specifically binds to the antigen with an affinity constant within about four-fold that of the donor immunoglobulin.

106. (New) A humanized immunoglobulin according to any one of claims 100 through 104, wherein said humanized immunoglobulin is an antibody tetramer, Fab, or $(Fab')_2$.

107. (New) A pharmaceutical composition comprising a humanized immunoglobulin according to any one of claims 100 through 104 and a pharmaceutically acceptable carrier.--

## REMARKS

This preliminary amendment is made to perfect the priority data in the specification. Also, with entry of this amendment, claims 1-85 have been canceled, and new claims 86-107 have been added. Support for the claims is replete throughout the specification.

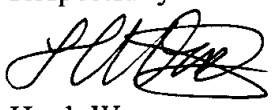
Support for "at least three" amino acid substitutions can be found, e.g., at page 5, lines 21-23 of the specification, and at page 4, lines 23-25 of the priority application U.S.S.N. 07/310,252 filed February 13, 1989. Support for "at least one of said amino acids is capable of interacting with CDRs 2 or 3" can be found, e.g., at page 200, lines 18-20 of original claim 1. In addition, the exemplary humanized anti-Tac antibody described, e.g., on pages 43-48 of the specification and on pages 21-28 of the priority application has at least three amino substitutions in the heavy chain framework outside the Kabat CDRs, and at least one of these (at positions 48 and 68; see page 43, lines 33-35) is capable of interacting with CDRs 2 or 3.

The specification also has support, e.g., at page 5, lines 3-27, for the recitation in the new claims that (1) the non-CDR amino acid to be substituted is adjacent to one of the CDRs; (2) the non-CDR amino acid to be substituted is capable of interacting with the CDRs; and (3) the donor amino acid is typical at its position for human immunoglobulin sequences, and the replaced amino acid is rare at its position for human immunoglobulin sequences. Support for the recitation that the humanized immunoglobulin has an affinity constant of $10^8 M^-$

and no greater than about 4-fold that of the donor immunoglobulin is found in the specification, e.g., at page 5, lines 33-35, and page 30, lines 16-18. The recitation of "antibody tetramer, Fab, or $(Fab')_2$" in the new claims has support in the specification, e.g., at page 26, lines 20-29. The recitation of "substantially pure" in the new claims has support in the specification, e.g., at page 40, lines 3-5. Support for the recitation of pharmaceutically acceptable carrier is found in the specification, e.g., at page 71, line 35 to page 72, line 3. Support for the recital of "at least 65%" or "at least 70%" sequence identity is found in the specification, e.g., at page 4, lines 17-20, and page 30, lines 16-18. The recitation of "at least 70" identical amino acids in the frameworks has support in the specification, e.g., at page 64, lines 8-11. Support for the recitation of alignment according to Kabat numbering has support in the specification, e.g., at page 36, lines 29-30, and page 127, lines 24-25. No new matter has been introduced by this preliminary amendment.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



Hugh Wang
Reg. No. 47,163

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: (415) 576-0200
Fax: (415) 576-0300